NEWS RELEASE

Immediate Release

Geneos Therapeutics Announces Positive Clinical Data for Personalized Therapeutic Cancer Vaccines in Ongoing Liver Cancer Trial

--Overall Response Rate 30.4 Percent in 23 Evaluable Patients Including Two Complete Responses and a Third Cancer-Free Patient--

--Vaccination-Related Adverse Events Limited to Grades 1 and 2 Only--

--100 Percent of Patients Analyzed Mount Tumor-Infiltrating CD4+ & CD8+ T Cells in Response to Vaccine Neoantigens; Validates Fundamental Effectiveness of Vaccination Methodology--

--Planning Underway for Potentially Registrational Clinical Trial--

Plymouth Meeting, PA—November 7, 2022—Geneos Therapeutics, a clinical stage biotherapeutics company focused on the development of personalized therapeutic cancer vaccines (PTCV), today announced positive safety and efficacy data from the first 24 patients (23 evaluable) enrolled in GT-30. GT-30 is an ongoing single-arm open-label multi-center Phase 1b/2a study to evaluate safety, immunogenicity, and efficacy of PTCV (GNOS-PV02) administered in combination with plasmid-encoded IL-12 (pIL12) and pembrolizumab in patients with unresectable or metastatic hepatocellular carcinoma (HCC) who progress on, or are intolerant to, first line tyrosine kinase inhibitors (sorafenib or lenvatinib). By RECIST1.1 an overall response rate of 29.2 percent in the modified intent-to-treat analysis (mITT) was observed, including complete responses in two patients as well as a third cancer-free patient who achieved secondary resectability and four additional partial responses. The data will be presented on November 10th in an oral presentation (Abstract #693) by clinical trial investigator, Edward Gane, MD, at the Society for Immunotherapy of Cancer (SITC) 37th Annual Meeting.

- To date, no dose limiting toxicities nor PTCV + pIL12 related serious adverse events (SAEs) or Grade 3 or 4 adverse events (AEs) have been reported. Grade 1 and 2 PTCV + pIL12 related AEs have been transient and mild.

- By RECIST1.1, disease control rate is 54.2 percent (13/24; mITT) consisting of two complete responses (CR), five partial responses (PR), six stable disease (SD) and 10 progressive disease (PD).
- A third patient (deemed a radiological PR) is cancer-free after a liver primary lesion and two lung metastases all reduced in size to become fully responsive to surgery and radiation therapy.
- One patient discontinued treatment due to a non-treatment-related SAE and was deemed unevaluable but included in the mITT analysis.
- Interferon gamma ELISpot assays showed the induction of PTCV neoantigen specific T cells in 22 of 22 evaluated patients post-vaccination.
- Novel and expanded T cell clones, predominantly CD8+ with activated phenotype, were identified in 100 percent of evaluated patients via pre-/post-vaccination analysis of T cell receptor (TCR) repertoire in peripheral blood and tumor tissue. These clones trafficked to the tumor microenvironment (TME) by week nine, potentially mediating the observed tumor regressions.

“As a physician who has been managing patients with advanced liver cancer for more than two decades, I am thrilled by the response rate and immunologic activity we are seeing with this promising form of therapeutic cancer vaccination,” stated Dr. Gane, professor of medicine at the University of Auckland, New Zealand, hepatologist and deputy director of the New Zealand Liver Unit at Auckland City Hospital. “To see three cancer-free patients out of 23 evaluable in second-line advanced HCC, with a treatment this well tolerated, tells me that personalized therapeutic cancer vaccination may now, finally, be here to stay. If these response rates are maintained as the program advances toward registration, then I see PTCV becoming a core foundation of cancer immunotherapy, not just for HCC, but broadly.”

“We're deeply gratified to see our PTCVs helping patients. The observation that all patients assessed mounted both a CD4+ and CD8+ T cell response to their own neoantigens means that our work to optimize all aspects of an ideal personalized therapeutic cancer vaccine, as well as its method of administration, has borne fruit. Cancer vaccination has always been a powerful idea and we believe these clinical data validate that with all of these technical pieces having come together, meaningful results are even achievable in advanced cancer settings,” stated Niranjan Sardesai, PhD, president and chief executive officer of Geneos. “In GT-30, manufacturing timing from biopsy to treatment is six to eight weeks but we have a clear path to reduce this to three to four. Doing so will make PTCVs practical for any cancer treatment setting, whether first-line or later-line, neoadjuvant, or adjuvant," Dr. Sardesai added.

GT-30 Trial of Geneos’ Personalized Therapeutic Cancer Vaccines

In the GT-30 trial, DNA plasmid-encoded personalized therapeutic cancer vaccine (PTCV) together with plasmid-encoded interleukin-12 (pIL12, a T cell-stimulating cytokine) are administered via intradermal injection followed by electroporation (EP) in combination with pembrolizumab. The potential utility of this combination was suggested by preclinical studies which demonstrate the ability of Geneos’ PTCV to rescue PD-1 in murine tumor therapeutic challenge models. Geneos’ PTCVs have been engineered to drive a strong CD8+ T cell response against the tumor. CD8 cells are the killing machines of the immune system, seeking out and destroying cancer cells, but have been difficult to induce using prior vaccine approaches. Adjuvant pIL12 and EP serve to optimize the effectiveness of peripheral vaccination, and their utility is seen by the effective CD4+/CD8+ T cell responses observed to the delivered neoantigens in the GT-30 patients. Meanwhile, each patient’s PTCV is designed

based on their unique tumor neoantigens (abnormal mutations and genomic variations produced by cancer cells) and unlike for other personalized platforms, in most every case, Geneos' PTCVs include all of a patient's specific neoantigens. This removes any requirement to try to pre-select the "high value" neoantigens accurately and, instead, leaves it to nature to decide which ones will matter for triggering a desired immune response.

Based on the 24-patient data, Geneos has expanded GT-30 to enroll a further 12 patients, with first reports on benchmark overall survival (OS) from the full cohort of 36 anticipated in mid-2023. In parallel, the company is developing plans for a potential registrational trial in advanced HCC with its medical advisors and preparing for discussion with regulatory agencies.

"While overall cancer rates are decreasing worldwide, HCC deaths are rising in the United States and globally, and the etiology of disease is shifting from viral to non-viral causes. HCC is resistant to immune checkpoint therapies in the majority of patients due to the largely immune excluded tumor microenvironment. Therapies that can bring CD8+ T cells into the tumor microenvironment, such as effective therapeutic cancer vaccines targeting cancer neoantigens, can reprogram the tumor microenvironment for checkpoint inhibitor therapy," stated Mark Yarchoan, MD, associate professor of oncology at Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, and clinical investigator on GT-30. "The promising data presented at this meeting lend optimism to the important role that PTCVs may play in cancer treatment."

Additional Geneos Abstracts at SITC Conference

Abstract #691 details a case study from GT-30 of a patient whose PTCV, designed based on the neoantigen content of a liver tumor primary lesion, resulted in a clinical PR. Profound shrinkage and control of the liver lesion resulted, now continuing for over a year. A metastatic adrenal lesion newly developed four months post initial treatment, the neoantigen content of which was similar but not identical to the liver primary lesion: while 16 of the original liver neoantigens remain, all four of the vaccine epitopes with strongest T cell responses were absent in the adrenal lesion. It is believed that this disappearance is an example, at exquisite immunologic detail, of immune pressure applied by a PTCV-induced T cell response. This case study confirms that tumor control, as well as the loss thereof, is being achieved by PTCV-directed immune responses and not by pembrolizumab alone, as no mechanistic theory of PD(L)-1 activity would explain these simultaneous clinical observations.

The ability to understand tumor progression at this level of immunologic detail also offers a credible vision for real world use of PTCV dynamic therapy to counter immune escape. It is straightforward to create a new PTCV in response to evolved neoantigen presentations, such as this patient's adrenal lesion, which would be co-administered with the original liver-targeted PTCV. Such evolved therapeutic vaccines could be a novel tool when new, or newly unresponsive lesions, present. These data will be presented in the poster session on November 10th by Dr. Yarchoan.

Abstract #692 summarizes the use of circulating tumor DNA (ctDNA) analysis in the GT-30 trial, to monitor tumor burden (progression or reduction). It was concluded that ctDNA may be a useful tool for monitoring disease in a patient specific manner. The ease of sample handling and analysis, and the rapid availability of data, may enable the use of ctDNA monitoring to allow real-time clinical treatment decision making for personalized cancer immunotherapy. These data

will be presented in the poster session on November 11th by Dr. Jian Yan, PhD, vice president, research and discovery at Geneos.

About Geneos Therapeutics

Geneos Therapeutics, a privately held, clinical stage biotherapeutics company, believes that the company's personalized therapeutic cancer vaccines (PTCVs) may serve an important role in new immunotherapeutic paradigms for cancer. The company's approach, using its proprietary GT-EPIC™ platform, is to target neoantigens (abnormal mutations produced by cancer cells) from individual patient tumors to develop novel and uniquely personalized treatments for cancer. Encouraging clinical data from a Phase 1b/2a clinical trial in hepatocellular carcinoma has prompted planning for a potentially registrational clinical trial. Geneos' experienced management team has a track record of success in building immunotherapy-based companies. For more information, please visit www.geneostx.com.

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This press release contains certain forward-looking statements relating to our business, including our plans regarding the development of personalized therapeutic cancer vaccines, our expectations regarding our research and development programs, including the planned expansion and conduct of clinical trials and the availability and timing of data from those trials, and the use of our capital resources. Actual events or results may differ from the expectations set forth herein. There can be no assurance that any product candidate in Geneos' pipeline will be successfully developed, manufactured or commercialized, that final results of clinical trials will be supportive of regulatory approvals required to market licensed products, or that any of the forward-looking information provided herein will be proven accurate. Forward-looking statements speak only as of the date of this release, and Geneos undertakes no obligation to update or revise these statements, except as may be required by law.